

# **Electromagnetic Biology and Medicine**



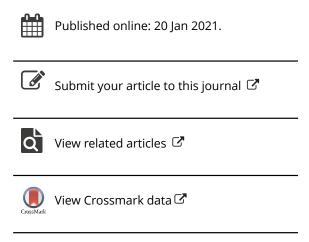
ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iebm20

# Association between reproductive health and nonionizing radiation exposure

Pooja Negi & Rajeev Singh

To cite this article: Pooja Negi & Rajeev Singh (2021): Association between reproductive health and nonionizing radiation exposure, Electromagnetic Biology and Medicine, DOI: 10.1080/15368378.2021.1874973

To link to this article: <a href="https://doi.org/10.1080/15368378.2021.1874973">https://doi.org/10.1080/15368378.2021.1874973</a>





#### **REVIEW**



## Association between reproductive health and nonionizing radiation exposure

Pooja Negia and Rajeev Singh (Da

<sup>a</sup>Department of Environmental Studies, Satyawati College, University of Delhi, Ashok Vihar, Delhi, India

#### **ABSTRACT**

Recently, a decreasing rate of fertility has to be credited to an array of factors such as environmental, health and lifestyle. Male infertility is likely to be affected by the strong exposure to heat and radiations. The most common sources of nonionizing radiations are cell phones, laptops, Wi-Fi and microwave ovens, which may participate to the cause of male infertility. One of the major sources of daily exposure to non-ionizing radiation is mobile phones. A mobile phone is now basically dominating our daily life through better services such as connectivity, smartphone devices. However, the health consequences are linked with their usage are frequently ignored. Constant exposure to non-ionizing radiations produced from a cell phone is one of the possible reasons for growing male infertility. Recently, several studies have shown that cell phone users have altered sperm parameters causing declining reproductive health. Cell phone radiation harms male fertility by affecting the different parameters like sperm motility, sperm count, sperm morphology, semen concentration, morphometric abnormalities, increased oxidative stress along with some hormonal changes. This review is focusing on the prevailing literature from in vitro and in vivo studies suggesting that non-ionizing exposure negatively affects human male infertility.

#### **ARTICLE HISTORY**

Received 7 October 2020 Accepted 6 December 2020

#### **KEYWORDS**

Nonionizing radiation; mobile phone; biological effects; male infertility; sperm; reproductive health

#### Introduction

Radiofrequency electromagnetic radiation (RF-EMR) is a kind of microwave radiation. Its dynamic properties integrate the recurrence at which it is created, estimated in megahertz (MHz) or gigahertz (GHz), and the intensity of the waves, or the specific absorption rates (SAR), which could be a degree of the rate of vitality exchange from the electromagnetic field to particles in an absorber, characterized at a specific point within the absorber (Durney 1986). One of the most significant exposures is in different types of electromagnetic radiation which is characterized into ionizing and non-ionizing radiation (NIR). The covalent bonds in biological molecules cannot be broken because of the very weak energy density of these EMFs and this kind of radiation exposure at the molecular level is known as NIR (Habash 2008).

Non-Ionizing Radiation indicates radiative energy that, rather than creating charged particles when going through matter, has adequate energy just for excitation but it is known to cause biological effects. The NIR range is separated into two main regions, optical radiations, and electromagnetic fields (Kwan-Hoong, 2003). One of the most popular devices we see today is people with their mobile phones close to their ears. These days we are taking cell phone technology as an agreed and required part of life and sadly disregarding the negative effects on our wellbeing. Cell phones use RF fields in the form of electromagnetic waves that are sent from the device to the closest base station for transmitting calls, text messages, emails, etc. (World Health Organization, 2014). Unlike ionizing radiations like X-rays or gamma rays, these RF waves cannot break chemical bonds nor are they strong enough to destroy our deoxyribonucleic acid (DNA). However, they are likely to be absorbed by tissues nearest to the site of exposure to the system and create a slight local thermal effect (Dhami 2011). The guidelines on the specific absorption rate (SAR) of cell phones are lawfully restricted to 2.0 W/kg by the International Commission Non-Ionizing Radiation Protection (ICNIRP) announced yet at the same time, the SAR level varies from nation to nation. SAR is a standard unit or rate at which RF-EMF energy is imparted to a component or mass to quantify the penetration of energy within human tissues (International Commission on Non-Ionizing Radiation Protection, 1998).

Mobile phones dually affect the human body and the interaction of EMFs electrical field and magnetic field outside of the biological system can never again be kept up inside the body because of the electrical and magnetic properties of living tissues. The human body functions as a parasitic antenna conveying the EMF from external sources (Habash 2008). The EM waves transmitted by

mobile phone relay wireless phone signals to antennas and base stations. Additionally, the magnetic field serves as another type of alternating mediated currents inside the human body. There has been rising concern and discussion in several countries about the declining male fertility in recent decades. To look into the causes of male infertility, it is important to know the harmful impact of lifestyle choices and factors that are commonly adapted. Many types of environmental and occupational exposure have been suggested as possible causes for the change in the infertility parameters (Skakkebaek et al. 2006). Occupational hazards are the best-documented risk factors for impaired male reproductive function and include physical exposures, chemical exposures, and processes of work such as metal welding (Bonde 2010). Radiation attained from mobile phones, tablets, Wi-Fi, and microwave ovens, since they are the most pervasive sources of non-ionizing radiation may lead to infertility by exploring the impact of radiofrequency radiation exposure on the pattern of male fertility. The networking of RF-EMF-aided devices is significantly increasing and its correlation with male infertility has been recorded (Kesari et al. 2010, Mcgrill et al. 2014). Many

studies of physiological and genetic environmental factors relating to male infertility seem to have been developed. Male infertility is largely associated with hazardous chemicals' exposure, ionizing radiation, RFradiation, and other environmental nuisance (Bin-Meferij et al. 2015).

## Mobile phone-induced general biological effects

The knowledge of how cell phone radiation can change natural body functions has been significantly developing. Many experiments investigated various responses to the exposure of radiation in body tissues. Changes were examined in the central nervous system, cardiovascular system, and also in the localized tissues. Cell phonegenerated radiofrequency electromagnetic radiation can improve brain excitability and has been identified as carcinogenic (Gupta et al. 2020: Merhi 2012). With improved handling of mobile phones, reduced mental activity, and melatonin secretion (D'Costa et al. 2003, Kramarenko and Tan 2003), variations in electroencephalograph (EEG) pattern, sleep rhythm, neuroendocrine

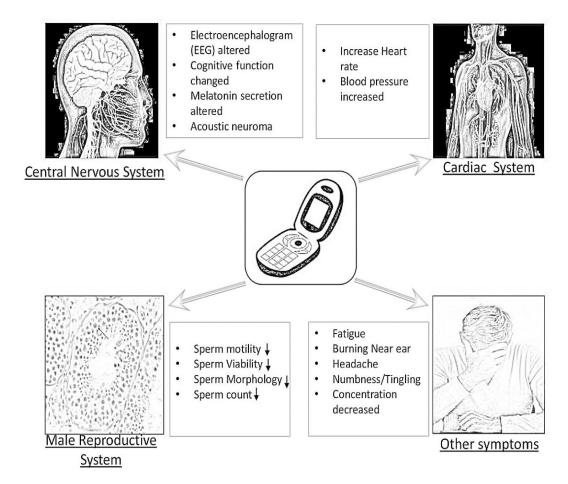


Figure 1. Potential health effects of mobile phone on the human body. (Source- Makkar et al. 2009)

functions and also correlated with attention and headache disorders have been reported (Figure 1). Exposure to mobile phones has also been found to raise resting blood pressure and raise heart rate (Kesari et al. 2010).

Regular users of mobile phones reported with concentration difficulties increased fatigue alongside a burning feeling near the ear and prickly or numbness of exposed tissue (Wdowiak et al. 2007) (Figure 1). Therefore, it can be observed that the mobile phone's impacts reach beyond the direct exposure period and that if amplified, these impacts will have a major impact on the user's health and well-being. Unfavorable effects of pregnancy along with abortion, stillbirth, premature puberty, altered gender ratio, and congenital abnormalities were all linked to exposure to maternal EMF. Health endpoints reported being associated with radiofrequency included childhood leukemia, brain tumors, genotoxic effects, neurological and neurodegenerative disorders, suppression of the immune system, infertility, and some cardiovascular effects. This also indicates that increased ROS (reactive oxygen species) plays an important role by improving the effect of radiation from microwaves that can cause neurodegenerative diseases (Kesari et al. 2013). Clinical work correlating EMF with adverse health results has often produced reputedly conflicting outcomes, study into sexual disease, most cancer capacity tends to assist previous concerns that exposure to EMF may pose a health risk. Revolutions in mobile phones show the antagonistic effects on the human biological system as the central nervous system, circulatory system, and more precisely reproductive system of the male (Makker et al. 2009; Singh et al. 2018).

## Mobile phone and male infertility

Infertility is a common disorder that affects 15% of couples and nearly half of the cases are due to male infertility. There are hazardous health effects of exposure to radiofrequency electromagnetic radiation emitted from mobile phones on the human reproductive pattern. There are many reports relating to the use of cell phones and harmful effects on the male reproductive system (Ribeiro et al. 2007). The mobile phone's radiated energy is absorbed by human body tissues and organs into which radiofrequency or resonant absorption penetrates seminiferous tubules (Agarwal et al. 2009). Many of these studies revealed that the key cause associated with these unexpected findings had to do with elevated

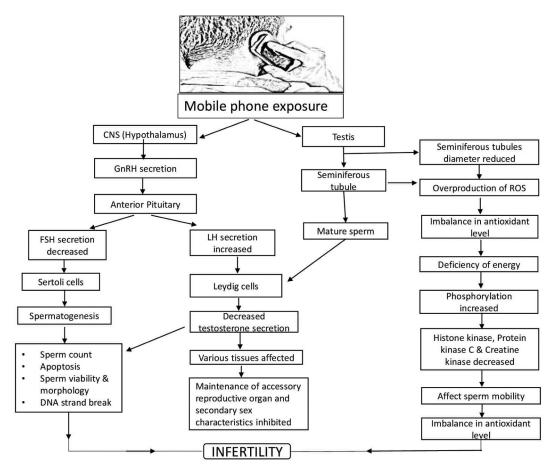


Figure 2. Possible correlations between mobile phone and male infertility.

Table 1. Summary of the major parameter of male infertility affected due to exposure.

S.No	Cell type	Source	Radiation exposure	Outcome	References
1.	Testicular cells	Rat	4 G Smartphone RF-EMR exposure at a different time, duration	Impaired testes and upregulates testicular gene Spock3, the establishment of sperm quality and testicular injury by inhibiting overexpression Spock3	Gang Yu et al. (2020)
2.	Testicular cells	Balb/c mice	2.4 GHz, SAR of 30 and 92 mW/kg	Sperm concentration (at a low power density of Wi-Fi radiation) significantly increased	Delavarifar S et al (2020)
3.	Spermatozoa	Mouse	905 MHz, SAR of 2.2 W/kg	Increased mitochondrial generation of ROS and DNA oxidation	Brendan et al (2019)
4.	Testicular cells	Male mice	905 MHz, SAR of 2.2 W/kg	Mitochondrial generation of ROS increased with elevated DNA oxidation	Houston et al. (2019)
5.	Testicular cells	Wistar rats	A dual-band (900 MHz,1800 MHz), SAR of 1.6 W/kg	Nonsignificant decrease in serum testosterone levels.	Okechukwu (2019)
6.	Germ cells	Swiss albino mice	(902.4 MHz and 0.250 W power), SAR of 0.0516 and 0.0054 W/kg	Cellular antioxidant (GSH) levels and anti-oxidative enzyme (SOD) activity shows a significant decrease	Pandey and Giri (2018)
7.	Leydig cells	Mouse	1950 MHz, 3 W/kg	Cell proliferation decreased, cell cycle distribution, Testosterone secretion capacity, and P450scc mRNA level reduced.	Yan-Yun Lir et al. (2017)
8.	Seminal fluid	Human	GSM1800/1900 MHz	Prolonged cell phone daily usage shows a decrease in motility ratio and progressive motility percentage	
9.	Spermatozoa	Rat	900 MHz, 0.66 ± 0.01 W/kg	Increases the ROS level and decreases TAC in sperm	Qi Liu et al (2015)
10.	Testicular cells	Rat	900 MHz	Sperm parameters decrease, irregular seminiferous tubules, giant multinucleated cells, and the number of Leydig cells reduced	Bin-Meferij et al (2015)
11.	Seminal fluid	Rat	2.45 GHz, 0.018 W/kg	Significant decrease in sperm count and sperm viability, Reduction in testicular $3\beta$ HSD activity and plasma testosterone levels	S.Shahin et al. (2014)
12.	Seminal fluid	Human	mobile phone	Sperm DNA fragmentation changed who use the mobile phone for more than 4 h/d $$	(2013)
13.	Testicular cells	Rat	2.45 GHz, SAR of 0.14 W/kg	Facilitate DNA Damage in testicular cells	Meena et.a (2013)
14.	Plasma Testosterone	Male Sprague Dawley rats	1800-MHz, SAR of 0.5762 W/kg	Regulation of testosterone affected	Qin F et al (2012)
15.	Spermatozoa	Human	900-MHz, SAR 2.0 W/kg	A significant effect on sperm morphometry, decrease in sperm binding to the Hemi zona	Falzone et al. (2011)
16.	Spermatozoa	Male Wistar rats	Mobile phone exposure, SAR of 0.9 W/kg	A decrease in sperm count and apoptosis increased	Kesari et al. (2010)
17.	Seminal fluid	Human	850 MHz, SAR of 1.46 W/kg	Motility and viability significantly reduced, Increased in ROS level while decreased in ROS-TAC score	Agarwal et al. (2009)
18.	Spermatozoa	Human	1.8 GHz, SAR from 0.4 to 27.5 W/kg	Decrease in sperm Motility and vitality while significantly increased in Mitochondrial ROS	
19.	Spermatozoa	Human	900 MHz GSM, SAR of 2.0 and 5.7 W/kg	Significant decrease in Mitochondrial membrane potential, no effect on motility	
20.	Seminal fluid	Human	Based on the mobile phone usage duration	Semen quality decreased, declining the sperm count, motility, viability	Agarwal et al. (2008)

oxidative stress within reproductive organs (Qin et al. 2012). There is a major decline in sperm motility and viability and an increase in human semen oxidative stress due to the emission of EM-RFR from mobile phones. A mobile phone on talk mode in a pocket of

the trouser may harm spermatozoa and hinder the fertility of males. Besides, EMW radiation can alter the functions of Sertoli cells, and Leydig cells, resulting in decreased hormone secretion consisting of folliclestimulating hormone that can lead to altered cell

proliferation (Agarwal et al. 2008; Roosli et al. 2007). The testis is one of the most susceptible tissues to the dangers of radiation that causes the testis to experience a significant firm impairment (Howell and Shalet 2005). The negative effects on testis function found by RF-EMR included enhanced blood test barrier, changes in the morphology of testicles, sperm number and sperm motility decreased, as well as alternation in DNA integrity of sperm or the endocrinal role (Aitken et al. 2005) (Figure 2). The key processes by which the damage is done are scrotal hyperthermia and oxidative stress (Depinder et al. 2007). The testicular temperature is known to be 2–3°C which is lesser than the temperature of the rectal, and it is assumed that the optimum temperature for spermatogenesis is 35°C. From this perspective, the practice of holding a mobile phone in or after the use of the trousers' pocket may also affect the potential hyperthermia generation and ROS (Saikhun et al. 1998). Furthermore, questions were raised about the transportation of mobile phones near reproductive organs, and most studies reported (Table 1) that mobile use cause sperm dysfunction; so, due to the deformation of Leydig and Sertoli cells which is associated with cell proliferation brings the changes in the cell cycle of sperm and leads to the decline in the men's fertility (Kesari et al. 2010).

# Mobile phone's effect on sperm parameters Semen quality

The frequency of the cellular component related to incoming waves and the resulting intensity of emitted may have an impact on the overall body as well as more critically on the male reproductive system. Cell phone use is turning out to be progressively famous around the world, with a definite group of the population assessed to use their mobile phone more than half of their day whether in standby or active mode. (Redmayne et al. 2011, Roberts et al. 2014). Due to the common habit of keeping cell phones near the testes, these people might be accidentally revealing their reproductive system to moderately significant levels of RF-EMR. This way it is an extensive concern that the utilization of cell phones and due to this exposure semen quality shows negative effects. (Agarwal et al. 2009; Fejes et al. 2005). All the given information supports the idea that NIR can fundamentally weaken crucial parts of sperm functions recommending an immediate impact on developing spermatozoa. Sperm DNA disintegration altogether changed in the groups exposed for more than 4 h in a day, specifically for the individuals keeping mobile phone in the pocket of their pants. (Rago et al. 2013).

Gutschi et al. (2011) examined in patients exposed to mobile phone radiation (Group A), the gametes with 68% had a compulsive morphology as compared to 58.1% in patients not exposed to mobile phone radiation (Group B). This exhibited that use of the mobile phone has a detrimental effect on men's sperm quality. A study by Jurewicz et al. (2009) concluded that cell phones badly harm the quality of semen by reducing sperm motility. Delavarifar et al. (2020) observed that the sperm concentration increases with the exposure of 2.4 GHz at SAR of 30 mW/kg and 92 mW/kg on testicular cells of Balb c mice.

#### Sperm motility

Several experiments have been performed that have looked at the adverse impact of mobile phones on sperm motility characteristics. Concerning the weakened motility nature of sperm, NIR appears to affect the sperm capacity to continue forward progressive motility. Certainly, Erogul and collaborators (2006) in their study concluded that the RF-EMR exposure for 5 min only to human sperm traded off their capacity to continue both moderated and quick progressive sperm motility (Erogul et al. 2006). Whereas some studies have used exposure for a long-time interval (hours/day) to produce a noteworthy decrease in motility and progressive motility of sperm appears to be the typical outcomes emerging from exposure of RF-EMR (Fejes et al. 2005). A prospective in vitro investigation of 32 individuals exposing the fresh semen samples to radiation (1.46 W/kg SAR for 60 min). Sperm motility and postexposure viability diminished altogether has been noticed by the researchers. It has been speculated that RF-EMR produced from mobile phones will rise oxidative stress in human spermatozoa bringing about a reduction in sperm motility and viability (Agarwal et al. 2009). It has been observed that testes impairment upregulates testicular Spock3 and inhibits Spock3 overexpression which restored the quality of sperm and testicular damage increased (Gang et al. 2020).

#### Sperm morphology

RF-EMW radiation from mobile phone use was also linked with a deterioration in normal sperm morphology. Data-based research was performed on 361 people to determine whether a link existed between mobile phone usage and morphology of sperm. Based on mobile phone usage subjects were grouped into no use, 4 h/d. A significant difference in mean normal sperm morphology between the group of low use  $(40.32 \pm 13.06)$  and the group of high-use (18.40 ± 10.38) was observed (Roosli et al. 2007). Wdowiak et al. (2007) have observed a substantial rise in the number of sperm with an uneven structure which is related to the amount and length of penetration radiofrequency radiation produced by mobile phones from GSM (Global Mobile Communications System). Patients with 55.6% showing that without mobile phones had standard morphology parameters (over 30% standard sperm morphology), while only 16.7% of the patients who used cell phones regularly (more than 2 years of daily phone use) had normal sperm morphology (Ofteda et al. 2005).

## Sperm number

The male fertilizing capability of sperm is adversely affected by the Radiofrequency radiation emitted from mobile phones or different sources of microwaves (Kumar et al. 2011). In an observational analysis, Fejes et al. (2005) found that a substantial decline in sperm count was related to the level of mobile phone treatment. This investigation examined 231 men more than 13 months and indicated that men use more mobile phones, sperm counts were 30% lesser than those who did not use for a long period. Haemocytometer, flow cytometry, and cell counter are many techniques used for the sperm count measurement. Utilizing Flowcytometry, Kesari et al. (2010) demonstrated in an animal study that fundamentally (p < 0.0001) diminished sperm count percentage (61.33 ± 3.68% versus  $31.14 \pm 13.6\%$ ) and a high percent of apoptotic cells  $(5.93 \pm 1.64\% \text{ versus } 13.15 \pm 1.26\%)$  after exposure from the mobile phone (2 h/d for 35 d). Such radiation exposure may generate a condition of free radical stimulation and oxidative stress produced by the sperm mitochondria (De Iuliis et al. 2009). In comparison, a study by Salama et al. (2003) rats exposed to RF-EMW mobile phone (2 h/d for 35 d at 0.9 W/kg SAR) in an experimental sample reported a reduced mean value of complete sperm count  $(31.14 \pm 13.6 \text{ vs. } 61.33 \pm 3.68)$  and an enhanced mean of apoptotic cells' percentage (13.15  $\pm$  1.26 vs. 5.93  $\pm$  1.64%). Research on rabbits exposed to cell phone radiation at GSM mode with 800 MHz radiation on standby status was also performed by Salama et al. (2010). RF-EMW treatment of 8 h/d resulted in a substantial drop in the count of sperm after 8 weeks of treatment and after exposure of 10 weeks, a decline in sperm motility.

#### Sperm capacitation and fertilization effects

Sperm capacitation and fertilization work under response to electromagnetic waves from mobile phones has not been broadly studied in the literature. However, hyperactivation motility parameters, particularly straight line or constant velocity, and BCF are hindered at a specific absorption rate of 5 W/kg (Falzone et al. 2008). This hyperactivation defect can result in a low rate of fertilization. In this experiment, the SAR value used was nevertheless greater than the current mobile phone's conventional SAR. Another study found that the thermal effects were not observed, as the temperature increase was just 0.38°C (Falzone et al. 2008). The effect on hyperactivation can be elucidated by EMW's effect on ROS, defects in DNA integrity, or loss of Ca2+. Likewise, another in vitro study by Falzone et al. (2011) on pure human sperm was not able to distinguish little varieties in untimely acrosomal reaction because of cell phone exposure with 900 MHz at SAR-2 W/kg for 60 min. The scientists, on the other hand, observed a substantial decrease in the binding of zona pellucida of sperm which correlated with a low rate of fertilization.

## Leydig cells

These are the interstitial testis cells with a critical role in promoting spermatogenesis and the male reproductive system, as they secrete 95% of the male testosterone under the Luteinizing Hormone effect (O'Shaughnessy et al. 2014). The secretion of testosterone is necessary to induce and maintain spermatogenesis. Several animal experiments have looked at the effect of EMW on the role of Leydig cells. In a report on mice, wang et al. (2003) found that Leydig cells are among the most exposed against EMW and that spermatogenesis can be disabled by harming these cells (Zhou et al. 2005). Oxidative stress and EMW mediated modification in the complex of PKC enzymes present in seminiferous tubules and behavior of Leydig cells may be disturbed in response to exposure to mobile phones. In this aspect, the application of RF-EMR radiation to mouse Leydig cells (TM3) resulted in the upregulation of Ets1 oncogene, giving in some studies a potential mechanism for interstitial disruption of cell function (Romano-Spica et al. 2000). In Leydig cell, pathological modifications such as vacuolation, cytoplasmic mitochondrial swelling, lipid droplet loss, light staining of most lipid droplets, and partial or full lipid droplet cavitation have been observed by Wang et al. within 28 d of EMW radiation (Wang et al. 2003). Khillare and Behari (1998) also observed after 35 d of exposure with 200 MHz RF fields and SAR 2.0-1.65 W/kg that there was no demonstrable modification in serum testosterone in male rats. The authors did find some ultrastructural changes in Leydig cells, however. On 35 d of exposure, Kesari and Behari (2010) stated due to microwave exposure at 2.45 GHz and 0.11 W/kg of SAR there is increased apoptosis in Leydig cells. In this analysis, an elevated apoptotic rate can be explained by different mechanisms, as defined under the context of biological interactions.

Besides, the analysis of the above information indicates that the impact of mobile phones on spermatozoa and related tissues is significant. However, the damage is not clear whether it is reversible or temporary or permanent, resulting in no demonstrable physiological changes in the actual radiation of the mobile phone. To analyze the harm based on uniform study procedure and graded response assessment, more work in this area is needed. Owing to a cell phone or microwave radiation, testicular infertility, or testicular cancer indicates an increased level of reactive oxygen species (ROS) also known as oxidation, which can also lead to DNA fragmentation. Besides, radiofrequency electromagnetic radiation generated from cell phones causes biological damage and results in many changes, such as decreased sperm count, enzymatic and hormonal changes, DNA damage, and apoptosis formation (Kesari et al. 2013). Human spermatozoa exposed to RF-EMR reduced sperm motility rate, and increased oxidative stress; and decrease in sperm concentration, normal morphology, and viability (La Vignera et al. 2012).

## Mobile phone-induced oxidative stress

Many findings indicate that the major cause leading to several unexpected effects inside the male reproductive organ was due to enhanced oxidative stress (Naziroglu et al. 2013). Studies also indicate that cell phones emit electromagnetic radiofrequency waves generating free radicals which ultimately leads to oxidative stress (De Luliis et al. 2009). Oxidative stress is a redox disequilibrium state in which the production of ROS contributes to a loss of the antioxidant defensive potential of the cell and results in DNA degradation and lipid peroxidation (Meena et al. 2014). Fenton reaction (iron-mediated process) triggered by exposure to mobile phone radiation is reported to cause severe damage to cells through increased free radical hydroxy formation (Kesari et al. 2013). The reproductive system of a male is extremely reactive to compartmentalized structure, to work properly involves the combination of intrinsic and extrinsic factors. ROS was considered as the primary causative agent of EMF disruption to spermatozoa from mobile phones (Hamada et al. 2011). Since spermatozoa plasma membranes are rich in polyunsaturated fatty acids, they are very prone to Reactive oxidative stress damage that results in lipid peroxidation. Lipid peroxidation affects spermatozoa's membrane integrity and motility (De Luliis et al. 2009). Brendan et al. (2019) and Houston et al (2019) explained that after 1 week of exposure the mitochondrial generation of ROS increased with the elevation in DNA oxidation and fragmentation. Radiofrequency electromagnetic radiation (RF - EMR) enhances human spermatozoa ROS production in mitochondria, which reduces its motility and viability and forms DNA base adduct (Aitken et al. 2006). The ROS caused by EMF adversely impacts the activity of antioxidant enzymes. It greatly influences the stability of the mitochondrial and nuclear genomes, and also induces apoptosis, degradation of DNA, and alters the expression of cytochrome c, Bax gene, etc. (Kesari et al. 2014, Kesari et al. 2011).

## Mobile phone exposure-induced hormonal changes

The seminiferous tubules are disturbed by RF exposure that reduced the testosterone serum concentration as the Leydig cell population decrease. Testosterone is secreted by Leydig cells where Leydig cells are stimulated by luteinizing hormone (LH) to produce and maintain testosterone functions. Testosterone is accountable for the LH secretion feedback control at both the hypothalamus hormone and pituitary hormone. This pituitary hormone helps in the testosterone secretion by the Leydig cells (Dohle 2010). Another analysis of rats by Ozguner et al. (2005) found that there is no considerable difference in FSH, LH, or interstitial histology but testosterone was substantially decreased in the group of EMR relative to the control group (p < 0.05). The study suggested that natural levels of FSH and LH could be explained by reduced anterior pituitary penetration to EMR contributing to low testosterone responding to the excessive release of FSH and LH (Ozguner et al. 2005). A substantial reduction in accessory sex glands was observed in rats when accessory sex glands androgen-dependent secretory activity exposed to cell phone radiation (Salama et al. 2009). Results were linked by the authors to potential differences in receptors of testosterone, or oxidative stress on male accessory glands (Salama et al. 2009).

## Mobile phone exposure-induced DNA integrity defects

Aside from a few other lifestyle factors, the use of the wireless device has been recognized to incite sperm DNA damage in men constantly using cell phones (Meena et al. 2014) as a result of an overproduction of responsive oxygen species (ROS). The development of various pathologies including tumors, and issues in the spermatogenesis may be prompted (Kumar et al. 2014). The vital functions of the sperm are control by the DNA as it contains genetic information. DNA damage from external and internal sources is correlated with poor semen quality and poor fertilization rate, as well as poor pregnancy outcomes (Zini et al. 2001). In both,



the nuclear and mitochondrial genomes of spermatozoa retrieved from the cauda epididymis showed DNA damage due to the RF-EMRs 7 d exposure in male mice (Aitken et al. 2005). TUNEL assay under cell phone EMW effect is proportional to the exposed SAR used for the detection of Sperm DNA integrity defects. De Iuliis et al. (2009) observed the rise in sperm DNA integrity defects. In contrast, Falzone et al. (2010) had used TUNEL assay under EMR exposure and did not find any significant DNA integrity defect in the sperm. Another in vitro study by Agarwal et al. (2009) failed to show any difference in EMR impact on sperm. These above studies conclude that EMW leads to DNA damage. However, this damage shows a collective effect due to long-term repeated exposure.

#### Conclusion

Generally, the outcome of the studies has indicated that mobile phone usage changes different sperm parameters in both ways in-vitro (human) and in-vivo (animals). Several studies disclose that the exposure to cell phones produces harmful effects on the testes, which may affect sperm motility, sperm number, sperm concentration, and morphology and an increased DNA damage, causing micronuclei formation and reactive oxygen species within the cell. So many evidences showed that exposure from cell phones results in elevated oxidative stress with disintegrated DNA and it is directly and indirectly dependent on the time of cell phone use. Further researches are required to provide strong evidence that the use of mobile phones may disturb sperm and testicular activity. Several evidences suggest that the irregularities reported due to RF-EMF-exposure depend on physical parameters such as utilized RF wavelength, penetration range into the object, and transmission length of the radiation. Unfortunately, existing studies are not able to suggest a true mechanism between the harmful effects of RF-EMF radiation and the male reproductive system. To conclude all of the above, government bodies and agencies should form strong guidelines against cell phone exposure and take preventive actions such as in the usage of mobile phones, preventing chatting, reducing the overall contact time, and holding the gadget away from the groin may be of significant help to people pursuing fertility. Moreover, very limited studies are available on protective actions so far so a large-scale analysis is also required to determine the reproductive parameters.

## **Acknowledgments**

We show the gratitude to the Indian Council of Medical Research, Delhi, for financial support for this review study.

## **Funding**

This review study is funded by the Indian Council of Medical Research, New Delhi. [5/10/FR/28/2019-RBMCH].

#### **ORCID**

Rajeev Singh (b) http://orcid.org/0000-0001-8804-155X

#### **Authors' contributions**

P N contributed majorly in the manuscript preparation. R S designed, analysed and corresponded the manuscript.

## Availability of data and materials

Not applicable.

#### **Declaration of interest**

The authors declare that they have no competing interests.

#### **List of Abbreviations**

Radiofrequency radiation (RF), Electromagnetic radiation (EMR), Electromagnetic radiofrequency radiation (EM-RFR), Specific absorption rate (SAR), Global System for Mobile Communications (GSM), Beat-cross frequency (BCF), Folliclestimulating hormone (FSH), Luteinizing hormone (LH), Reactive oxygen species (ROS).

#### References

Agarwal, A., F. Deepinder, R. K. Sharma, G. Ranga, and J. Li. 2008. Effect of cell phone usage on semen analysis in men attending infertility clinic: An observational study. Fertil. Steril. 89:124-28. doi:10.1016/j.fertnstert.2007.01.166.

Agarwal, A., N. R. Desai, K. Makker, A. Varghese, R. Mouradi, E. Sabanegh, and R. Sharma. 2009. Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: An in vitro pilot study. Fertil. Steril. 92:1318-25. doi:10.1016/j.fertnstert.2008.08.022.

Aitken, R. J., L. E. Bennetts, D. Sawyer, A. M. Wiklendt, and B. V. King. 2005. Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline. Int. *J. Androl* 28:171–79. doi:10.1111/j.1365-2605.2005.00531.x.

Bin-Meferij, M. M., and A. F. El-Kott. 2015. The radioprotective effects of Moringa oleifera against mobile phone electromagnetic radiation-induced infertility in rats. Int. J. Clin. *Exp. Med* 8:12487–97.

Bonde, J. P. Mar 2010. Male reproductive organs are at risk from environmental hazards. Asian J. Androl. 12:152-56. doi: 10.1038/aja.2009.83.



- D'Costa, H., G. Trueman, L. Tang, U. Abdel-Rahman, W. Abdel-Rahman, K. Ong, and I. Cosic. 2003. Human brain wave activity during exposure to radiofrequency field emissions from mobile phones. Aust. Phys. Eng. Sci. Med. 26:162-67. doi:10.1007/BF03179176.
- De Iuliis, G. N., R. J. Newey, B. V. King, and R. J. Aitken. 2009. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in PLoSONE4:e6446. doi:10.1371/journal. pone.0006446.
- Delavarifar, S., Z. Razi, A. Tamadon, F. Rahmanifar, D. Mehrabani, M. Owifard, O. Koohi-Hpseinabadi, and S. Zaker Abasali. 2020. Low-power density radiations emitted from common wi-fi routers influence sperm concentration and sperm histomorphometric parameters: Anew horizon on male infertility treatment. I Biomed Phys Eng 10:167-76. doi:10.31661/jbpe.v0i0.581.
- Depinder, F., K. Makkler, and A. Agarwal. 2007. Cell phones and male infertility: Dissecting the relationship. Reprod. Biomed. Online 3:266-70. doi:10.1016/S1472-6483(10) 60338-0.
- Dhami, A. K. 2011. Study of electromagnetic radiation pollution in an Indian city. Environ. Monit. Assess. 184:6507-12. doi:10.1007/s10661-011-2436-5.
- Dohle, G. R. 2010. Male infertility in cancer patients: Review of the literature. *Int. J. Urol.* 17:327–31. doi:10.1111/j.1442-2042.2010.02484.x.
- Durney, C. 1986. Radiofrequency Radiation Dosimetry Handbook. 4th ed. UT, USA: The University of Utah Salt
- Erogul, O., E. Oztas, I. Yildirim, T. Kir, E. Aydur, G. Komesli, I. H C, I. M K, and P. A F. 2006. Effects of electromagnetic radiation from a cellular phone on human sperm motility: An in vitro study. Arch Med Res. 2006 Oct;37(7):840-3.
- Falzone, N., C. Huyser, D. R. Franken, and D. Leszczynski. 2010. Mobile phone radiation does not induce pro-apoptosis effects in human spermatozoa. Radiat. Res. 174:169-76. doi:10.1667/RR2091.1.
- Falzone, N., C. Huyser, F. Fourie, T. Toivo, D. Leszczynski, and D. Franken. 2008. In vitro effect of pulsed 900 MHz GSM radiation on mitochondrial membrane potential and motility of human spermatozoa. Bioelectromagnetics 29:268-76. doi:10.1002/bem.20390.
- Falzone, N., C. Huyser, P. Becker, D. Leszczynski, and D. R. Franken. 2011. The effect of pulsed 900-MHz GSM mobile phone radiation on the acrosome reaction, head morphometry and zona binding of human spermatozoa. Int. Androl. 34:20-26. doi:10.1111/j.1365-J. 2605.2010.01054.x.
- Fejes, I., Z. Za'vaczki, J. Szo"llosi, S. Kolosza'r, J. Daru, and P. A. Kova'csL. 2005. Is there a relationship between cell phone use and semen quality? Arch. Androl. 51:385-93. doi:10.1080/014850190924520.
- Gupta, S., R. S. Sharma, and R. Singh. 2020. Non-ionizing radiation as possible carcinogen. Int J Environ Health Res 1–25. doi:10.1080/09603123.2020.1806212.
- Gutschi, T., B. Mohamad Al-Ali, R. Shamloul, K. Pummer, and H. Trummer. 2011. Impact of cell phone use on men's semen parameters. J. Andrologia 43:312-16. doi:10.1111/ j.1439-0272.2011.01075.x.
- Habash, R. W. Y. 2008. Bioeffects and therapeutic applications of electromagnetic energy. Boca Raton: CRC Press.

- Hagras, A. M., E. A. Toraih, and M. Fawzy. 2016. Mobile phones electromagnetic radiation and NAD+-dependent isocitrate dehydrogenase as a mitochondrial marker in asthenozoospermia. Biochim Open. 25;3:19-25.
- Hamada, A. J., A. Singh, and A. Agarwal. 2011. Cell phones and their impact on male fertility: Fact or fiction. Open Reproductive Science Journal 5:125–37.
- Houston, B. J., B. Nixon, K. E. McEwan, J. H. Martin, B. V. King, R. J. Aitken, and G. N. De Iuliis. 2019. Whole-body exposures to radiofrequency-electromagnetic energy can cause DNA damage in mouse spermatozoa via an oxidative mechanism. Sci Rep 9: doi: 10.1038/s41598-019-53983-9.
- Howell, S. J., and S. M. Shalet. 2005. Spermatogenesis after cancer treatment: Damage and recovery. J. Natl. Cancer Inst. Monographs 34:12–17. doi:10.1093/jncimonographs/ lgi003.
- International Commission on Non-Ionizing Radiation Protection. 1998. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). International Commission on Non-Ionizing Radiation Protection.. Health physics 74:
- Jurewicz, J., W. Hanke, M. Radwan, and J. P. Bonde. 2009. Environmental factors and semen quality. Int J Occup Med Environ Health 22:305-29. doi:10.2478/v10001-009-0036-1.
- Kesari, K. K., and J. Behari. 2010. Microwave exposure affecting reproductive system in male rats. Appl. Biochem. Biotechnol 162:416-28. doi:10.1007/s12010-009-8722-9.
- Kesari, K. K., R. Meena, J. Nirala, J. Kumar, and H. N. Verma. 2014. Effect of 3G cell phone exposure with computer controlled 2-D stepper motor on non-thermal activation of the hsp27/p38MAPK stress pathway in rat brain. Cell Biochem. Biophys. 68:347-58. doi:10.1007/s12013-013-9715-4.
- Kesari, K. K., S. Kumar, and J. Behari. 2010. Mobile phone usage and male infertility in Wistar rats. Indian J. Exp. Biol. 48:987-92.
- Kesari, K. K., S. Kumar, and J. Behari. 2011. Effects of radiofrequency electromagnetic wave exposure from cellular phones on the reproductive pattern in male Wistar rats. Appl. Biochem. Biotechnol. 164:546-59. doi:10.1007/s12010-010-9156-0.
- Kesari, K. K., S. Kumar, J. Nirala, M. H. Siddiqui, and J. Behari. 2013. Biophysical evaluation of radiofrequency electromagnetic field effects on male reproductive pattern. Cell Biochem. Biophys. 65:85-96. doi:10.1007/s12013-012-9414-
- Kesari, KK ,Behari J. 2010. Effects of microwave at 2.45 GHz radiations on reproductive system of male rats. Toxicoll Environ Chem 92:1135-47. doi:10.1080/02772240903233637.
- Khillare B, Behari J. 1998. Effect of amplitude-modulated radiofrequency radiation on reproduction pattern in rats. Electromagn Biol Med 17:43-55.
- Kramarenko, A. V., and U. Tan. 2003. Effects of high-frequency electromagnetic fields on human EEG: A brain mapping study. Int. J. Neurosci. 113:1007-19. doi:10.1080/00207450390220330.
- Kumar, S., J. P. Nirala, J. Behari, and R. Paulraj. 2014. Effect of electromagnetic irradiation produced by 3G mobile phone on male rat reproductive system in a simulated scenario. Indian J. Exp. Biol. 52:890-97.
- Kumar, S., K. K. Kesari, and J. Behari. 2011. The therapeutic effect of a pulsed electromagnetic field on the reproductive



- patterns of male Wistar rats exposed to a 2.45-GHz microwave field. Clin (Sao Paulo) 66:1237-45. doi:10.1590/S1807-59322011000700020.
- Kwan-Hoong, N. (2003). Non-ionizing radiations-sources, biological effects, emissions and exposures, proceedings of the international conference on non-ionizing radiation at UNITEN (ICNIR2003) Kualalampur, Malasia Electromagnetic Fields and Our Health.
- La Vignera, S., R. A. Condorelli, E. Vicari, R. D'Agata, and A. E. Calogero. 2012. Effects of the exposure to mobile phones on male reproduction: A review of the literature. J. Androl. 33:350–56. doi:10.2164/jandrol.111.014373.
- Makker, K., A. Varghese, N. R. Desai, R. Mouradi, and A. Agarwal. 2009. Cell phones: Modern man's nemesis? Reprod. Biomed. Online 18:148-57. doi:10.1016/S1472-6483(10)60437-3.
- Meena, R., K. Kumari, J. Kumar, P. Rajamani, H. Verma, and K. K. Kesari. 2014. Therapeutic approaches of melatonin in microwave radiations-induced oxidative stress-mediated toxicity on male fertility pattern of Wistar rats. Electromagn Biol Med 33:81-91. doi:10.3109/15368378.2013.781035.
- Merhi, Z. O. Apr 2012. Challenging cell phone impact on reproduction. J. Assist. Reprod. Genet. 29:293-97. doi: 10.1007/s10815-012-9722-1.
- Naziroglu, M., M. Yuksel, S. A. Kose, and M. O. Ozkaya. 2013. Recent reports of Wi-Fi and mobile phone-induced radiation on oxidative stress and reproductive signaling pathways in females and males. J. Membr. Biol 246:869-75. doi:10.1007/s00232-013-9597-9.
- O'Shaughnessy, P. J., A. Monteiro, P. A. Fowler, and I. D. Morris. 2014. Identification of Leydig cell-specific mRNA transcripts in the adult rat testis. Reproduction 147:671-82. doi:10.1530/REP-13-0603.
- Okechukwu, C. E. 2019. Effects of mobile phone radiation and exercise on testicular function in male wistar rats. J. Exp. Clin. Biosci. 6:51. doi:10.4103/njecp.njecp\_18\_18.
- Ozguner, M., A. Koyu, G. Cesur, M. Ural, F. Ozguner, A. Gokcimen, and N. Delibas. 2005. Biological and morphological effects on the reproductive organ of rats after exposure to electromagnetic field. Saudi Med J 26:405–10.
- Pandey, N., and S. Giri. 2018. Melatonin attenuates radiofrequency radiation (900 MHz)-induced oxidative stress, DNA damage and cell cycle arrest in germ cells of male Swiss albino mice. Toxicol Ind Health 34:315-27. doi:10.1177/0748233718758092.
- Qin, F., J. Zhang, H. Cao, C. Yi, J. X. Li, and J. Nie. 2012. Effects of 1800-MHz radiofrequency fields on circadian rhythm of plasma melatonin and testosterone in male rats. J. Toxicol. Environ. Health Part A 75:1120-28. doi:10.1080/ 15287394.2012.699846.
- Rago, R., P. Salacone, L. Caponecchia, A. Sebastianelli, I. Marcucci, A. E. Calogero, R. Condorelli, E. Vicari, G. Morgia, V. Favilla, et al. 2013. The semen quality of the mobile phone users. J Endocrinol Invest. 36(11):970-4.
- Redmayne, M., E. Smith, and M. J. Abramson. 2011. Adolescent in-school cell phone habits: A census of rules, survey of their effectiveness, and fertility implications. Reprod Toxicol; 32(3):354-9.
- Ribeiro, E. P., E. L. Rhoden, M. M. Horn, C. Rhoden, L. P. Lima, and L. Toniolo. 2007. Effects of subchronic exposure to radiofrequency from a conventional cellular

- telephone on testicular function in adult rats. J. Urol. 177:395–99. doi:10.1016/j.juro.2006.08.083.
- Roberts J A., Y. L H, and C. Manolis. 2014. The invisible addiction: Cell-phone activities and addiction among male and female college students. Journal of Behavioral Addictions 3254-65.
- Romano-Spica, V., N. Mucci, C. L. Ursini, A. Ianni, and N. K. Bhat. 2000. Ets1 oncogene induction by ELFmodulated 50 MHz radiofrequency electromagnetic field. Bioelectromagnetics 21:8-18. doi:10.1002/(sici)1521-186x (200001)21:1<8::aid-bem3>3.0.co;2-g.
- Roosli, M., G. Michel, C. E. Kuehni, and A. Spoerri. 2007. Cellular telephone use and time trends in brain tumour mortality in Switzerland from 1969 to 2002. Eur. J. Cancer Prev. 16:77-82. doi:10.1097/01.cej.0000203618.61936.cd.
- Saikhun, J., Y. Kitiyanant, V. Vanadurongwan, and K. Pavasuthipaisit. 1998. Effects of sauna on sperm movement characteristics of normal men measured by computer-assisted sperm analysis. Int. J. Androl. 21:358-63. doi:10.1046/j.1365-2605.1998.00138.x.
- Salama, N., T. Kishimoto, and H. O. Kanayama. 2010. Effects of exposure to a mobile phone on testicular function and structure in adult rabbit. Int. J. Androl. 33:88-94. doi:10.1111/j.1365-2605.2008.00940.x.
- Salama, N., T. Kishimoto, and K. S. Kanayama H-O. 2009. The mobile phone decreases fructose but not citrate in rabbit semen: A longitudinal study. Syst. Biol. Reprod. Med. 55:181-87. doi:10.3109/19396360903013126.
- Singh, R., R. Nath, A. K. Mathur, and R. S. Sharma. 2018. Effect of radiofrequency radiation on reproductive health. Indian J. Med. Res. 148 2018 Dec:S92-S99. doi:10.4103/ ijmr.IJMR\_1056\_18.
- Skakkebaek, N. E., N. Jorgensen, K. M. Main, E. R.-D. Meyts, H. Leffers, A.-M. Andersson, A. Juul, E. Carlsen, G. Mortensen, T. K. Jensen, et al. 2006. Is human fecundity declining? Int. J. Androl. 29:2-11. doi:10.1111/j.1365-2605.2005.00573.x.
- wang, S.-M., D. Wang, R.-Y. Peng, Y.-B. Gao, Y. Yang, W.-H. Hu, H.-Y. Chen, Y.-R. Zhang, and Y. Gao. 2003. Effect of electromagnetic pulse irradiation on structure and function of Leydig cells in mice. Zhonghua Nan Ke Xue 9:327-30.
- Wdowiak, A., L. Wdowiak, and H. Wiktor. 2007. Evaluation of the effect of using mobile phones on male fertility. Ann. *Agric. Environ. Med.* 14:169–72.
- World Health Organization. 2014. Fact Sheet No. 193. Electromagnetic Fields and Public Health: Mobile Phones. Geneva. Available on: https://www.who.int/news-room/ fact-sheets/detail/electromagnetic-fields-and-publichealth-mobile-phones(Accessed on-17/08/2020)
- Yu, G., Z. Tang, H. Chen, Z. Chen, L. Wang, H. Cao, ... Z. Bai Science of The Total Environment, 133860 (2020). Long-term exposure to 4G smartphone radio frequency electromagnetic radiation diminished male reproductive potential by directly disrupting Spock3-MMP2-BTB axis in the testes of adult rats.
- Zhou, W., X. B. Wang, J. Q. Yang, Y. Liu, and G. B. Zhang. 2005. Influence of electromagnetic irradiation on P450scc mRNA expression in rat testis tissues and protective effect of the shield. *Zhonghua Nan Ke Xue* 11:269–71.
- Zini, A., K. Kamal, D. Phang, J. Willis, and K. Jarvi. 2001. Biologic variability of sperm DNA denaturation in infertile men. Urology 58:258-61. doi:10.1016/S0090-4295(01)01180-3.